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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/699,224	10/27/2000	Peter A. Rice	BOS/3	8386

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/699,224	RICE ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12,13 and 15-31* is/are pending in the application.

4a) Of the above claim(s) *17-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 12, 13, 15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: Sequence search report (one page)

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicants' submission filed on 09/13/04 has been entered.

Applicants' Amendments

2) Acknowledgment is made of Applicants' amendments filed 09/13/04 and 10/21/04 in response to the Office Actions mailed 11/12/03 and 03/12/04.

Status of Claims

3) Claims 1, 2 and 6 have been amended via the amendment filed 10/21/04.

Claims 1-10, 12, 13 and 15-31 are pending.

Claims 1-10, 12, 13, 15 and 16 are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) Maintained

6) The objection to the drawings made in paragraph 6 of the Office Action mailed 02/26/03 under 37 C.F.R 1.84 is maintained for reasons set forth therein.

Rejection(s) Withdrawn

7) The rejection of claims 1, 3, 9, 10, 12, 13 and 15 made in paragraph 10 of the Office Action mailed 02/26/03 and maintained in paragraph 12 of the Office Action mailed 11/12/03 and paragraph 12 of the Office Action mailed 03/12/04 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 6 of the US patent

5,476,784 ('784); claims 1-9 and 11 of US patent 5,939,067 (Rice *et al.*) ('067), and claims 1-4 of the US patent 6,099,839 (Rice *et al.*) ('839), is withdrawn in light of Applicants' amendment to the claims and/or the base claim(s).

8) The rejection of claim 2 made in paragraph 12(d) of the Office Action mailed 02/26/03 and maintained in paragraph 15 of the Office Action mailed 11/12/03 and paragraph 13 of the Office Action mailed 03/12/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

9) The rejection of claim 6 made in paragraph 12(e) of the Office Action mailed 02/26/03 and maintained in paragraph 16 of the Office Action mailed 11/12/03 and paragraph 14 of the Office Action mailed 03/12/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

10) The rejection of dependent claims 4-10 and 15 made in paragraph 12(f) of the Office Action mailed 02/26/03 and maintained in paragraph 17 of the Office Action mailed 11/12/03 and paragraph 15 of the Office Action mailed 03/12/04 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

11) The rejection of claims 1, 3, 9, 10, 12 and 13 made in paragraph 15 of the Office Action mailed 02/26/03 and maintained in paragraph 19 of the Office Action mailed 11/12/03 and paragraph 16 of the Office Action mailed 03/12/04 under 35 U.S.C. § 102(e) or 102(a) as being anticipated by Rice *et al.* (US 5,939,067) ('067), is withdrawn in light of Applicants' amendment to the base claim and Applicants' arguments.

12) The rejection of claims 1, 3, 9, 10, 12 and 13 made in paragraph 16 of the Office Action mailed 02/26/03 and maintained in paragraph 20 of the Office Action mailed 11/12/03 and paragraph 17 of the Office Action mailed 03/12/04 under 35 U.S.C. § 102(b) as being anticipated by Rice *et al.* (US 5,476,784) ('784), is withdrawn in light of Applicants' amendment to the base claim and Applicants' arguments.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

13) Claims 2, 4-10, 12, 13, 15 and 16 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which

Applicants regard as the invention.

(a) Claim 2 is vague and confusing in the recitation 'the amino acid sequence of the peptide mimic comprises the sequence SEQ ID NO: 8'. For clarity and for the purpose of distinctly claiming the subject matter, it is suggested that Applicants replace the limitation with --the peptide mimic comprises the amino acid sequence of SEQ ID NO: 8--.

(b) Claim 5 is vague and lacks proper antecedent basis in the limitation 'said sequence' (see line 2). For proper antecedence, it is suggested that Applicants replace the limitation with --said amino acid sequence--.

(c) Claim 16 is vague in the limitation 'peptide mimic comprising the peptide sequence' (see line 2). For proper antecedence, it is suggested that Applicants replace the limitation with --peptide mimic comprising the amino acid sequence--.

(d) Claims 12 and 13 are vague and indefinite in the limitation: 'peptide mimic binds to a monoclonal antibody', because it is unclear whether or not the binding is immunospecific or non-specific.

(e) Claim 13 is vague and indefinite in the limitation 'fragment thereof', because it is unclear what is encompassed in this limitation. What constitutes a fragment, and how much of the monoclonal antibody's original structure has to be retained such that the resulting product can be considered a 'fragment' is not clear. The metes and bounds of the structure encompassed in the limitations 'fragment' are indeterminate.

(f) Claim 13 is vague and indefinite in the limitation 'HB 11311' because it is unclear what does it represent. Is this a hybridoma cell line?

(g) Claims 4-10 and 15, which depend directly or indirectly from claim 2, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C § 102

14) Claims 1, 3-6, 8 and 15 are rejected under 35 U.S.C § 102(b) as being anticipated by Magdalene *et al.* (WO 85/04654).

It is noted that the instant specification describes the 'peptide mimic' to include a peptide. See lines 1-6 of page 12 of the specification.

Magdalene *et al.* disclosed an isolated peptide smaller than the naturally-occurring gonococcal pilin protein, preferably five to twenty amino acids in length, or about 20 to about 35 amino acids in length containing an epitope, which immunologically mimicks a conserved antigenic determinant site in the carboxy-terminal half of a gonococcal pilin protein and which elicits IgG antibodies (i.e. T-cell dependent immune response) in a mammalian host (see abstract; pages 3 and 5, lines 9-28; lines 1-10 on page 6; lines 16-26 of page 7; paragraph bridging pages 12 and 13; second full paragraph on page 13; page 23, first full paragraph; pages 29 and 33; and claims 11 and 12). The peptide can contain a cysteine residue at its termini which can be bonded together by intramolecular, interpolypeptide disulfide bonds, i.e., to form a cyclic peptide (see second and third full paragraphs on page 18; last full paragraph on page 7; pages 4 and 8; and paragraph bridging pages 13 and 14; and page 14), and can be produced as a fusion protein, i.e., being coupled to a second agent (see first full paragraph on page 19). The peptide can be linked or conjugated to a carrier or second agent, such as, bovine serum albumin, tetanus toxoid, KLH, and the like (see lines 13-30 of page 13). The peptide-containing vaccine comprises a pharmaceutically acceptable carrier and an adjuvant, such as, alum or Freund's adjuvant (see second full paragraph on page 19; and page 21). The peptide in the vaccine is present in 10 to 100 milligram quantities, i.e., immunoprophylactically effective amount (see first full paragraph on page 20; and paragraph bridging pages 12 and 13). The prior art peptide is viewed as the same as the instantly claimed conserved gonococcal peptide since the prior art peptide is not described Magdalene *et al.* as being present on human blood group antigens.

Claims 1, 3-6, 8 and 15 are anticipated by Magdalene *et al.*

15) Claims 1, 2, 10 and 15 are rejected under 35 U.S.C § 102(b) as being anticipated by Kufer *et al.* (WO 98/46645 A2).

Kufer *et al.* taught a 13 amino acid-long synthetic peptide having the amino acid sequence of DESGLF, which is 100% structurally identical to the instantly recited amino acid sequence of SEQ ID NO: 8. See the attached sequence search report; Example V; and item 39 in Table 3 of Kufer *et al.* Since the prior art peptide is a synthetic peptide, it inherently serves as an isolated peptide. Kufer *et al.* taught a composition comprising the peptide and a buffer (see page 41).

Although Kufer *et al.* are silent about the peptide being a mimic of a conserved gonococcal epitope that is not found on human blood group antigens and about its ability to induce an immune response in a mammal to said epitope or its ability to compete with gonococcal LOS for binding to 2C7 monoclonal antibody, the prior art peptide is viewed as the same as the Applicants' peptide mimic. The Office's position that Kufer's peptide is the same as the Applicants' peptide is based upon the fact that the structure of Kufer's peptide and the structure of Applicants' peptide mimic are the same. There is 100% structural identity between the prior art peptide and Applicants' peptide mimic having SEQ ID NO: 8. Therefore, in spite of the fact that Kufer *et al.* fail to teach all of Applicants' disclosed characteristics of the peptide, there is sufficient overlap to reasonably conclude that Kufer's peptide is one and the same as the Applicants' peptide mimic. Since the prior art peptide is structurally the same as the Applicants' peptide mimic, for example the one recited in claim 2, it is expected not to be found on human blood group antigens; is expected to have the capability to induce an immune response in a mammal against a conserved gonococcal epitope; and is expected to bind 2C7 monoclonal antibody, or the monoclonal antibody produced by the hybridoma recited in claim 13. The capacity to induce an immune response in a mammal against a conserved gonococcal epitope is viewed as an inherent property inseparable from the peptide of Kufer *et al.*

Claims 1, 2, 10, 12, 13 and 15 are anticipated by Kufer *et al.*

Rejection(s) under 35 U.S.C § 103

16) Claim 7 is rejected under 35 U.S.C § 103(a) as being unpatentable over Magdalene *et al.* (WO 85/04654) as applied to claim 6 above and further in view of Clements (*Inf. Immun.* 58: 1159-1166, 1990).

The teachings of Magdalene *et al.* are explained above, which do not disclose the second agent that is coupled to the peptide mimic to be an adjuvant.

However, it was routine and conventional in the art at the time of the invention to fuse an art-known adjuvant to an art-known peptide to enhance peptide's immunogenicity. For instance, Clements taught genetically fusing *E. coli* LT-B (i.e., an adjuvant) to a peptide antigen to produce a hybrid molecule (i.e., fusion protein) in order to enhance the antibody production of the peptide (see

abstract; page 1159; Materials and Methods; and Results).

Given the express teaching of Magdalene *et al.* that their conserved gonococcal peptide can be produced as a fusion protein, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to fuse or couple Magdalene's conserved gonococcal peptide to Clements' *E. coli* LT-B adjuvant to produce the instant invention with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of further enhancing the prior art peptide's immunogenicity as taught by Clements.

Claim 7 is *prima facie* obvious over the prior art of record.

17) Claim 9 is rejected under 35 U.S.C § 103(a) as being unpatentable over Magdalene *et al.* (WO 85/04654) as applied to claim 1 above and further in view of Tam (*In*: *Peptide Antigens*: *A Practical Approach*. (Ed) Wisdom G.B. IRL Press, Oxford University Press, New York, pp. 83-90. 1994), or Huang *et al.* (*Mol. Immunol.* 31: 1191-1199, 1994).

The teachings of Magdalene *et al.* are explained above, which do not disclose the peptide mimic being a part of a multiple-antigen peptide or MAP.

However, it was routine and conventional in the art at the time of the invention to modify a peptide as a multiple antigen peptide with a built-in-adjuvant for the purpose of providing a very high density of the peptide epitope. For instance, see the teachings of Tam on pages 87, 83 and 84.

Huang *et al.* taught the disadvantage of presenting a peptide as a peptide-protein carrier or as an adjuvant mixture, the disadvantage being the difficulty in defining the chemical composition and stoichiometry of such a mixture. Huang *et al.* taught the advantages of presenting a peptide via a MAP system. Huang *et al.* taught that the MAP system permits the amplification of antigens 4- to 8-fold to attain a macromolecule and avoids the use of a protein carrier as well as attendant structural ambiguity. See page 1191.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify Magdalene's conserved gonococcal peptide mimic as a multiple antigen peptide with a built-in-adjuvant as taught by Tam, to produce the instant invention, with a reasonable expectation of success. One of skill in the art would have been motivated to

SEQ ID NO. 8

```
RESULT 2
AAW80858
ID   AAW80858 standard; peptide; 13 AA.
XX
AC   AAW80858;
XX
DT   16-FEB-1999  (first entry)
XX
DE   Amino acid sequence of the synthetic peptide 41.
XX
KW   Synthetic peptide; human; receptor; antigen; tumour; auto-immune disease;
KW   PCR; primer; graft rejection; allergy; inflammatory disease;
KW   endocrine disease; degenerative disease.
XX
OS   Synthetic.
XX
PN   WO9846645-A2.
XX
PD   22-OCT-1998.
XX
PF   14-APR-1998;   98WO-EP002180.
XX
PR   14-APR-1997;   97EP-00106109.
XX
PA   (KUFE/) KUFER P.
PA   (RAUM/) RAUM T.
XX
PI   Kufer P,  Raum T;
XX
DR   WPI; 1998-594564/50.
XX
PT   Production of anti-human antigen receptors - by selecting a combination
PT   of functionally rearranged VH and VL immunoglobulin chains expressed from
PT   a recombinant vector.
XX
PS   Example 5; Page 40; 84pp; English.
XX
CC   This is the amino acid sequence of a synthetic peptide used in the method
CC   of the invention, involving the identification of receptors that can be
CC   used for targeting antigens in humans without being immunogenic
CC   themselves. Such receptors can be used for treating diseases such as
CC   tumours or auto-immune diseases, graft rejection after transplantation,
CC   infectious diseases by targeting cellular receptors as well as allergic,
CC   inflammatory, endocrine and degenerative diseases by targeting key
CC   molecules involved in the pathological process
XX
SQ   Sequence 13 AA;

  Query Match             96.4%;  Score 27;  DB 2;  Length 13;
  Best Local Similarity   83.3%;  Pred. No. 9.4;
  Matches    5;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 DEXGLF 6
              || |||
Db          4 DESGLF 9
```

produce the instant invention for the expected benefit of presenting Magdalene's conserved gonococcal peptide mimic as a multiple antigen peptide with a built-in-adjuvant for the purpose of advantageously providing a very high density of the peptide mimic as taught by Tam, or for avoiding the use of a protein carrier and avoiding structural ambiguity of the conjugate as taught by Huang *et al.*

Claim 9 is *prima facie* obvious over the prior art of record.

Remarks

18) Claims 1-10, 12, 13, 15 and 16 stand rejected. Claim 16 contains allowable subject matter.

19) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300.

20) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

21) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

January 05

S. DEVI, PH.D.
PRIMARY EXAMINER